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<p>(54) Title: A COMPLIANCE METER FOR CLINICAL EVALUATION OF DRUGS</p> <div data-bbox="722 1312 1161 1575"> </div> <p>(57) Abstract</p> <p>A device for sensing and signalling the removal of a tablet from a blister pack includes an insulating sheet in which holes (20) are provided for each tablet location. Disposed around each hole are a series of electrical contact surfaces (10, 11) which are mutually so connected that each alternate surface is coupled to a first signal conductor (100) and the remainder are coupled to a second signal conductor (110-112). When a tablet is removed from the pack, the thus broken aluminium foil will establish an electric contact between the system of electrodes (10, 11).</p>		

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A COMPLIANCE METER FOR CLINICAL EVALUATION OF DRUGS.

When evaluating the usefulness of drugs, it is necessary to carry out lengthy and costly trials to establish their effectiveness and also to establish any side-effects that they might have. In fact, it is not possible to register new drugs and medicaments with government authorities unless usefulness and a reasonable absence of side-effects can be shown.

A particular difficulty encountered in trials of this nature derives from the so-called placebo effect, which enables a patient to be helped, both subjectively and even objectively, with the aid of "sugar pills", provided that the patient believes that he has been administered with an effective drug. It is doubtful that drugs can be effectively tested against the effect of placebos, unless the doctor concerned is also unaware of which tablets contain the placebo and which contain the active drug, since otherwise the doctor may inadvertently divulge to the patient, in some way or another, the fact that a particular tablet is nothing more than a placebo. The practice of double blind trials is therefore widespread and necessary.

An idea of the difficulties encountered when testing drugs is given by the clinical observation that a patient administered with a placebo may also complain of side-effects resulting therefrom. In the case of one reported study in which patients were administered with placebos, no less than a quarter of the patients concerned discontinued taking the placebo, because of the side-effects felt to be caused thereby (Capel et al, J. Rheumatol. 6 (1979) 584-593).

The standard procedure in clinical drug trials is to supply the patients concerned with blister cards or charts containing the drug in tablet form, together with a prescription as to how many tablets should be taken and at what times. The patient is also instructed to make notes relevant to the treatment. This is particularly important in the case of short-lived drugs, such as pain relieving drugs. One problem with such practises is that the patient may forget to make notes at the times prescribed and attempt to rectify this omission at a later date, for instance immediately prior to seeing his doctor. Cases are also known where a patient who has forgotten to take his tablets, removes a few from the blister chart and throws them away, thus pretending to have taken the tablets and therewith avoiding the doctor's displeasure.

Consequently, it is an object of this invention to provide a compliance meter with which many of the pitfalls experienced in drug trials can be avoided. By compliance is meant here the strict obedience of the patient in following the doctor's instruction as to the times when the drugs (tablets) are to be taken and in what quantities, or, in a relative sense, how the tablets were taken and when, in those cases, for instance, when the patient was told to take a tablet when and if the need was felt.

In accordance with the invention, this and other objects are realized by means of a compliance meter set forth in claim 1.

Known to the art are devices which signal to a patient when a tablet should be taken and which stop signalling

when the tablet is removed from the pack, these devices functioning in the manner of an alarm clock.

5 Some devices of this kind are constructed to receive a blister pack and means are provided for detecting when a blister pad is broken and a tablet is freed therefrom, whereupon the "alarm clock" is switched off and is not restarted until the next time a tablet is to be taken. Examples of such devices are to be found in DE-A-33 35  
10 301 and EP-A-0 191 168.

Although such devices have been found practical from the aspect of patient treatment, thereby overcoming the forgetfulness of old or very sick patients, they are  
15 not particularly useful for the purpose of the present invention.

One particularly important advantage afforded by the present invention is that it is ~~thereby made possible~~  
20 ~~to register the time at which a tablet is taken from the blister pack and also the tablet which was taken at that time.~~ This is of particular value when the tablets concerned are a mixture of different tablets and, for instance, comprise placebo tablets. For example, when  
25 testing the effect of pain relieving tablets which the patient or subject is allowed to take at will, it is extremely valuable to know the length of time which passes before a further tablet is taken and also how this length of time varies with the type of tablet  
30 taken. In accordance with the inventive concept, these times are stored in a memory so as to enable them to be analyzed, therewith providing results which could hardly be otherwise obtained at reasonable cost.

In accordance with the invention, the device comprises a blister card holder, means for pressing a tablet from the card, and an electric sensor located at each tablet position. Devices of this kind are known to the art, e.g. from the aforesaid patent publications.

According to one preferred embodiment of the invention, the aluminium foil which is normally present in such blister packs is used to make a connection between electric contacts located in the pack holder.

According to one important feature of the invention, all of the tablet locations can be sensed and a removed tablet identified. Preferably, a conductor or lead is drawn from each tablet location to a selector network, such as to allow the tablets or tablet locations to be sensed individually. This is of particular advantage when the aluminium foil present is used as a means of making electric contact, since once made the contact can be maintained indefinitely. When using individual holder-mounted electric contact devices or switches which are arranged so as to be activated only when a tablet is pushed from the pack, it may be possible instead to use a multiplexed sensing system and thereby to limit the number of input leads to one set of column leads and one set of row leads, as will be understood by those skilled in this art.

According to one advantageous embodiment, the inventive device is provided with a lid provided with holes which correspond to the tablet positions, which lid may either be collapsible or, together with the contact-carrying card, form a pocket which will enable a blister pack to be inserted from one side.

The device may also be provided with a code reading facility which is effective in reading a code on the package. This code may have the form of a bar code, or a margin

notch or recess code capable of being sensed by micro-switches, which in other respects may be coordinated with those electrical contact elements or switches which are closed automatically as the blister pack is opened.

According to one beneficial application, the inventive device is coupled to a computer equipped with a text screen and a keyboard or button bank through which a patient is able to answer questions concerning his condition, e.g. the level of pain felt, the computer being able to store both the drug intake of the patient and the result achieved, which greatly enhances the level of reliability, since the test is no longer reliant on the memory of the patient or his ability to make notes, especially when the patient is weakened by sickness. The use of such an auxiliary arrangement supplemented to a greater or lesser degree, in cases of regular treatment, can also be effective in so reducing the extent of personal care as to enable patients who might otherwise need to be hospitalized to be cared for in their homes.

The invention will be understood more readily from the following description of an exemplifying, non-limiting embodiment thereof.

Figure 1 illustrates the principle of the known blister pack.

Figure 2 illustrates the manner of removal of tablets from a blister pack according to Figure 1.

5        Figure 3 shows part of a blister pack mounted in a device according to the invention.

Figure 4 shows part of a circuit card.

10       Figure 5 illustrates a perforated circuit card provided with sensing electrodes.

Figure 6 illustrates an electronic circuit for sensing a device according to the invention.

15       Figure 7 illustrates an inventive device with a blister pack mounted therein.

20       A tablet 4 packed in a blister pack is shown in Figure 1. The blister pack has a first plastic layer 1, which is normally transparent, and which has pressed therein recesses or alveoli 3 in which tablets 4 are placed. The alveoli are covered with aluminium foil 2 which is secured with an adhesive. When the foil is depressed by the finger in the direction of the arrow 5, the layer is deformed and the tablet 4 will be pushed through the aluminium foil 2, which deforms, bulges outwardly and subsequently ruptures. Figure 3 illustrates a type of blister pack in which the said layers are placed between two pieces of perforated cardboard 6 and 7, which is particularly suitable in respect of the present invention. According to the invention, when in use the blister pack lies on a sheet 12 of insulating material provided with holes which lie opposite the locations of respective tablets. Electrodes 10 and 11 are located at

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the edges of the holes. When the blister pack is broken open, as illustrated in Figure 2, the aluminium foil will make electric contact with the electrodes 10 and 11. In those cases when the blister pack lacks a cardboard sheet, it will be necessary to include a cardboard insert, in order to ensure that a space is obtained between the foil 2 and the electrodes 10 and 11.

Figure 5 illustrates a plate for a blister pack containing 28 tablet sites or locations, there being 20 holes at each tablet location. The positioning of the electrodes and the requisite circuitry will be seen best from Figure 4. A multiple of electrodes, here 14, are arranged around the holes 20 and are connected such that all alternate electrodes, the electrodes 10, are mutually connected to a common first signal conductor, which will normally be earthed, via a grid net arranged on the same side of the plate, which will normally be a circuit card. The remaining electrodes, referenced 11, are mutually connected at each tablet site or location to a conductor on the rear side, via metallised holes, and form a multiple of second signal conductors, such as 110, 111 and 112 in Figure 4, the number of second signal conductors being equal to the number of tablet locations.

Thus, when a tablet is removed from the pack, an electrical contact is established between the first signal conductor 100 and one of the second signal conductors, e.g. the conductor referenced 110 in Figure 4 when the tablet is removed from the tablet location 50 shown in the top left quadrant of Figure 4.

Figure 6 illustrates schematically the manner in which these "switches" are used, one for each tablet. For the

sake of simplicity in illustration, only one such "switch" 50 has been shown, although it will be understood that the number provided may equal the number of tablet locations.

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The circuitry illustrated in Figure 6 incorporates five integrated circuits 60-63 and 70 of the kind designated HC 151 (Motorola).

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These integrated circuits each have eight signal inputs, three address inputs and one output. Logic circuits ensure that for each possible digital address, i.e. eight addresses, the state of one of the signal inputs is sensed (high or low), and the output will then show a correspondingly high or low value. It will be seen from the Figure that the "switch" 50, which corresponds to a tablet location, will normally function as an open switch, prior to taking a tablet from the pack. In this state of the switch, the other signal conductor of the switch is not connected to earth, but has a high level due to being connected to positive voltage +V, via a resistance 51. The other signal conductor is connected to one of the unmarked signal inputs on the circuit 60.

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Each of all other signal conductors from the remaining tablet locations (not shown) is connected to a respective signal input on one of the circuits 60, 61, 62 or 63. The device illustrated in Figure 6 is thus able to accommodate other signal conductors, to a total of 32.

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A computer 75 is provided for reading all "switches", such as 50. In operation, digital signals are transmitted on six parallel outputs a-f. The three least significant bits d, e and f, are connected to the three

address inputs on the circuits 60, 61, 62 and 63. Each of the outputs A, B, C, D of these circuits 60, 61, 62 and 63 is connected to a respective signal input on the circuit 70, which is of the same type as the others.

5 Thus, a signal input on each of the circuits 60-63 is indicated through the three least significant bits d, e, and f, and if, for instance, the illustrated "switch" 50 is closed (tablet removed), the output signal A from this switch will be high when indicated by the bits d, e and f. When the bits a, b and c, which are connected to  
10 the circuit 70, then indicate the input A, a high signal will pass to the computer.

The computer is programmed to address the bit sites or  
15 locations in sequence, for instance every tenth of a second. If a tablet signals that the "switch" is closed, the computer leaves the search loop and repeats the indication towards the signalled tablet location, e.g. seven times, in order to make absolutely certain that  
20 the tablet has been removed and the switch closed, whereafter the identity of the tablet removed and the time of its removal are stored in the memory of the computer.

25 The program may suitably be such that once a tablet has been removed, the computer will no longer include this particular location in its periodic search.

In accordance with a preferred embodiment, the inventive  
30 device also includes four microswitches 80-83, which are activated by the edge of the pack upon its insertion. For instance, said edge may have provided therein an opening which when located opposite one of the microswitches, causes the switch to be open, whereas the  
35 switch is closed in the absence of such an opening. In

this way, 14 mutually different configurations can be recognised ("all open" will signal the absence of the pack, whereas "all closed" will signal that an uncoded and wrong tablet pack has been inserted)

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The sensing arrangement illustrated in Figure 6 is only an example of a conceivable circuit for sensing or detecting the removal of a tablet from the pack, and it will be understood that many other circuit embodiments are conceivable. This also applies to the coding possibilities, which can be effected in other ways, e.g. through bar codes (e.g. type EAN) capable of being read when the package is inserted.

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Figure 7 illustrates a device 90 constructed in accordance with the invention, and shows a blister pack 91 being inserted into the device through an open flap 92. The tablet alveoli are available through holes 93, the released tablets falling through holes (not shown) located in the undersurface of the device. The device incorporates a light signal in the form of a signalling lamp 95 and an acoustic signal in the form of a buzzer 94, which will remind a patient that a tablet should be taken, ingested. Although not shown, the device may be provided with means which enables it to be connected to a data collecting computer, either permanently or temporarily during a visit from the doctor concerned.

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Figure 7 also shows a coding example. The blister pack of this embodiment has formed therein two recesses 96, which as the pack is inserted into the device adjust the mutual positions of two contact arms of microswitches. When, e.g., a further two microswitches are present, their reading value will be the opposite and therewith enable the blister pack to be identified.

Claims

1. A device for signalling the ingestion of medic-  
5 aments in tablet form packed in so-called blister packs  
in which the various tablet compartments on one side are  
delimited by means of a foil sheet which is common to  
the pack as a whole, characterised in that the device is  
intended for standard type blister packs of the kind in  
10 which said foil (2) is a metal foil; in that the device  
includes a sheet (12) of insulating material having  
provided therein holes (20) which are so arranged as to  
correspond to the positions of the tablets in the pack;  
in that electrodes (10, 11) having an electrically  
15 conductive surface are disposed circumferentially around  
each hole on one side of the sheet; in that a first  
number (10) of these electrodes are mutually connected  
to a first signal conductor, whereas a second number of  
said electrodes are mutually connected to a second  
20 signal conductor; in that the foil (2) is arranged such  
that when a tablet is removed through a hole in the  
blister pack located in the device, an electric contact  
is made between an electrode of the said first number of  
electrodes (10) and an electrode of the second number of  
25 electrodes (11) and therewith establish an electric  
connection between the first and the second signal  
conductors.

2. A device according to claim 1, characterised in  
30 that the first conductors from all of said first number  
of electrodes (10) of the holes (20) are mutually con-  
nected to a common first signal conductor (100), whereas  
the second signal conductors (110, 111, 112) from the  
various holes (20) are each connected to a respective  
35 input of a sensing circuit (Fig.6).

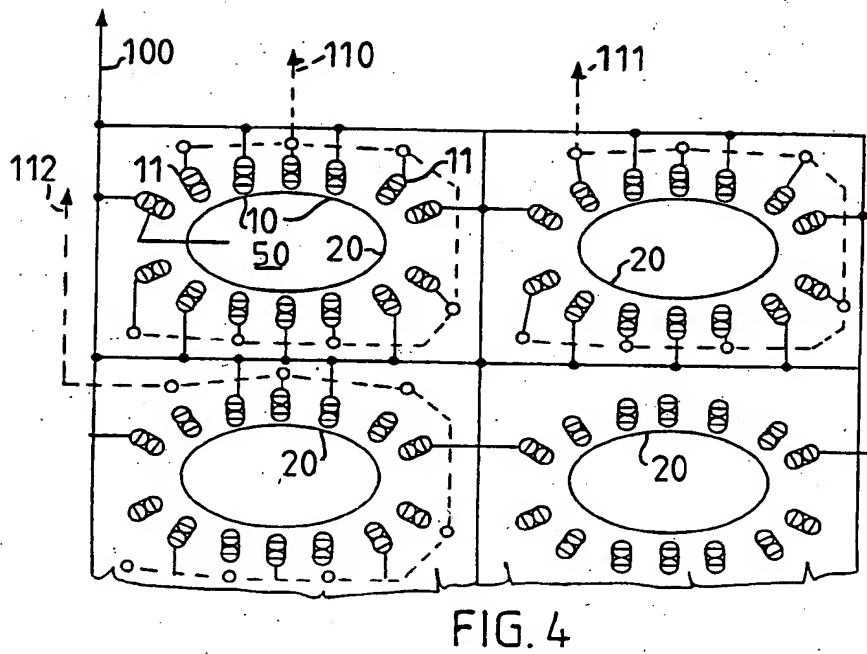
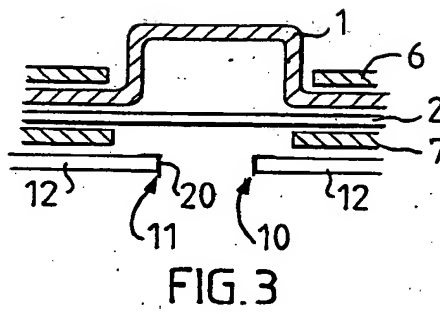
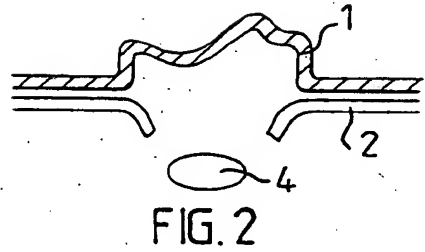
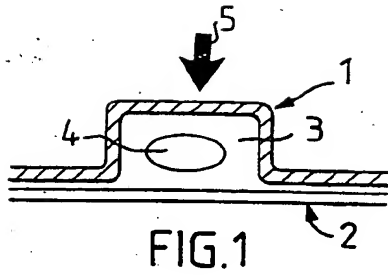
3. A device according to claim 2, characterised in  
that in that the insulating sheet is a circuit card  
5 which has conductors drawn on both sides thereof and in  
which the first number of electrodes (10) are connected  
to the common first signal conductor, at least essen-  
tially through conductors drawn on one side of the circ-  
uit card, whereas the second number of electrodes (11)  
10 are connected to the inputs of the sensing circuit at  
least partly through conductors drawn on the other side  
of the circuit card.

4. A device according to claim 2, characterised in  
15 that the sensing circuit includes for each second signal  
conductor a resistor (50), one end of which is connected  
to voltage source (+V), and an input of a sensing cir-  
cuit (60-63); in that a multiplex device is provided for  
sensing the states of the various amplifiers, and in  
20 that with each detected change of state in respective  
circuits, corresponding to a short circuit between a  
first (10) and a second (11) signal conductor, a signal  
(71) is sent to a detecting computer (75).

25 5. A device according to claim 1, characterised by a  
code reading arrangement (80-83) for reading a code  
provided on the blister pack..

6. A device according to claim 5, characterised in that  
30 the code reader comprises a plurality of contact devices  
which are intended to be influenced by the presence and  
absence of recesses (96) in an edge margin of the  
blister pack.

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SUBSTITUTE SHEET

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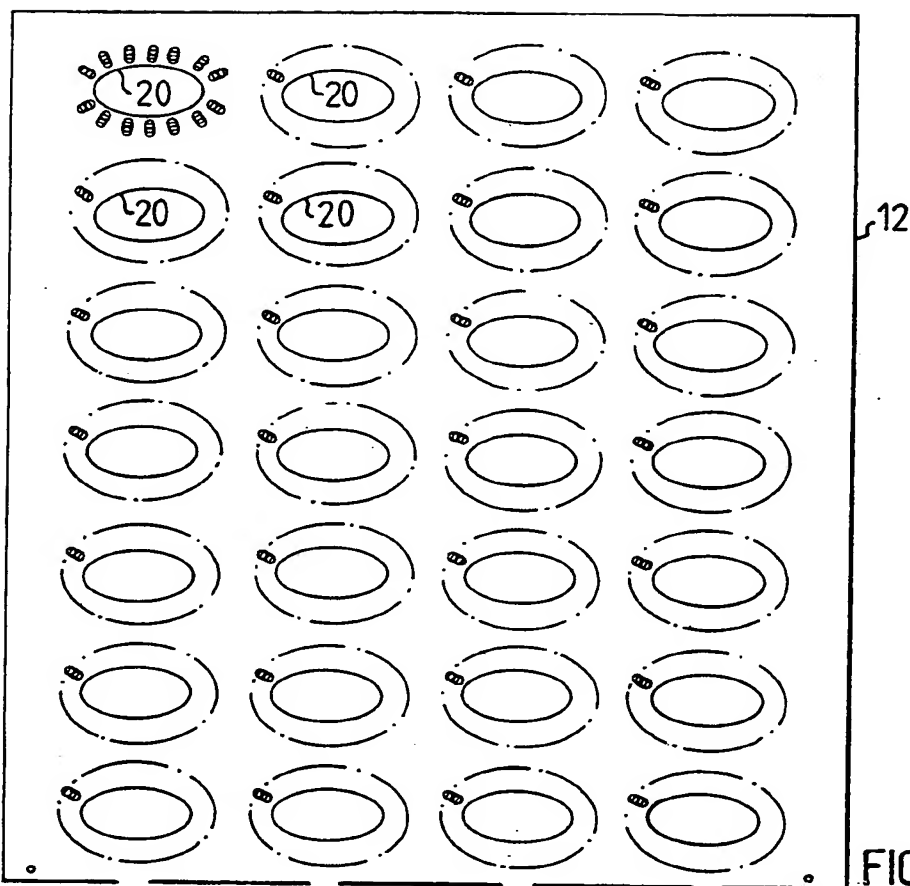


FIG. 5

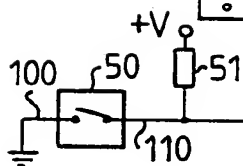
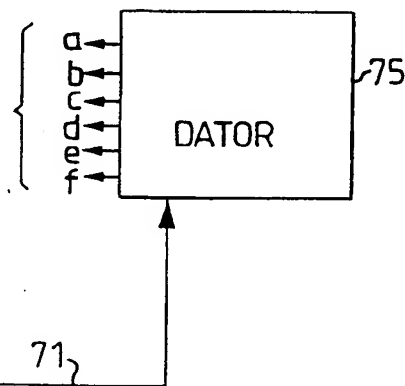
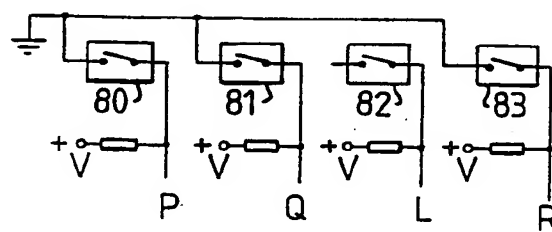
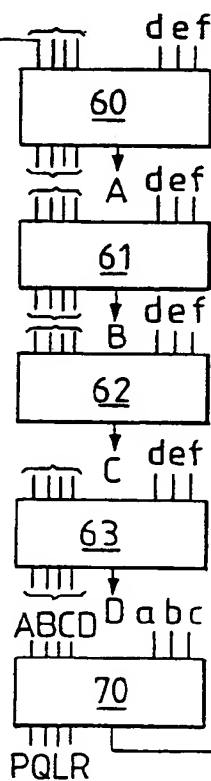


FIG. 6



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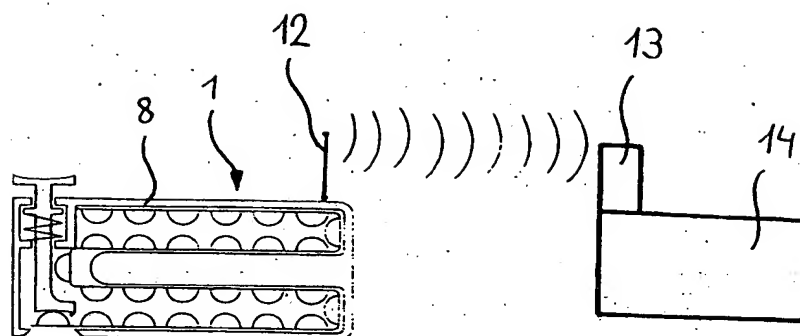


Fig. 6

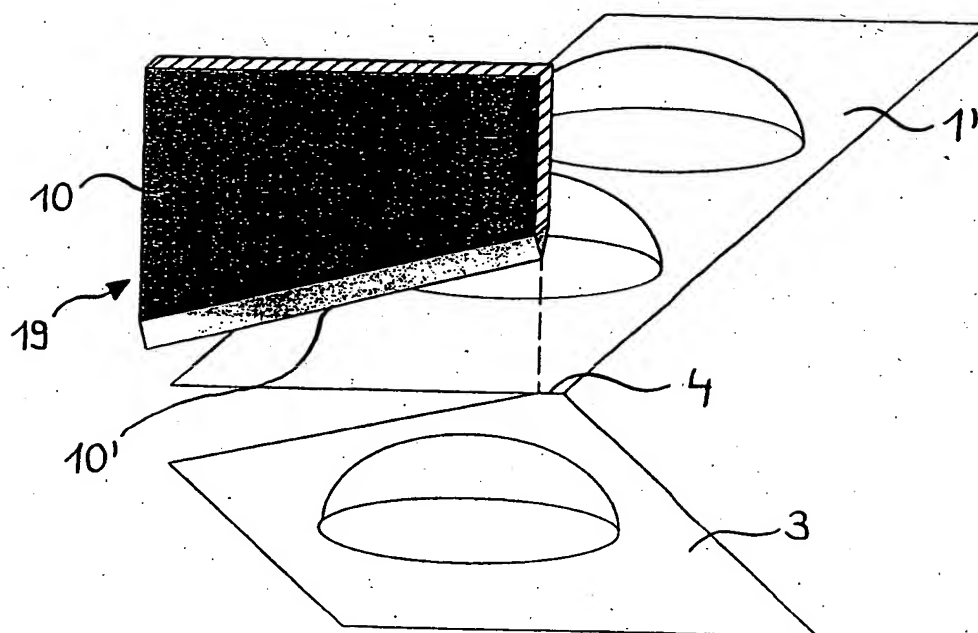


Fig. 9

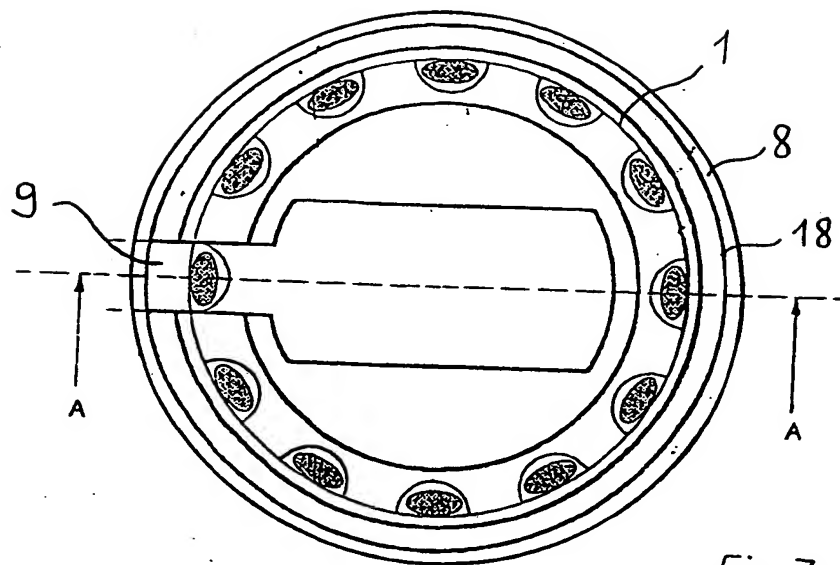


Fig. 7

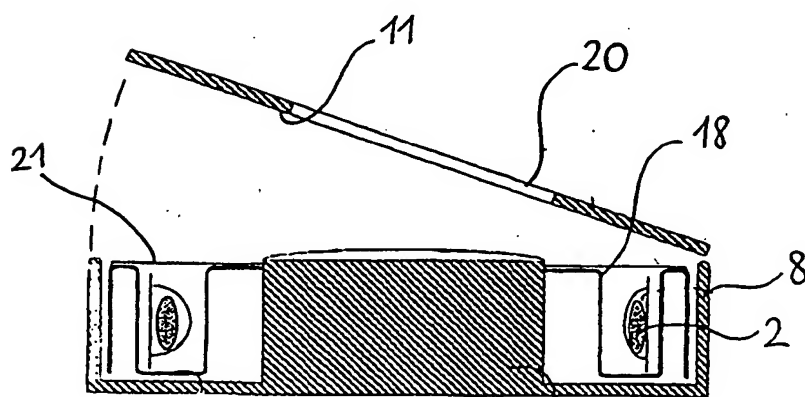


Fig. 8

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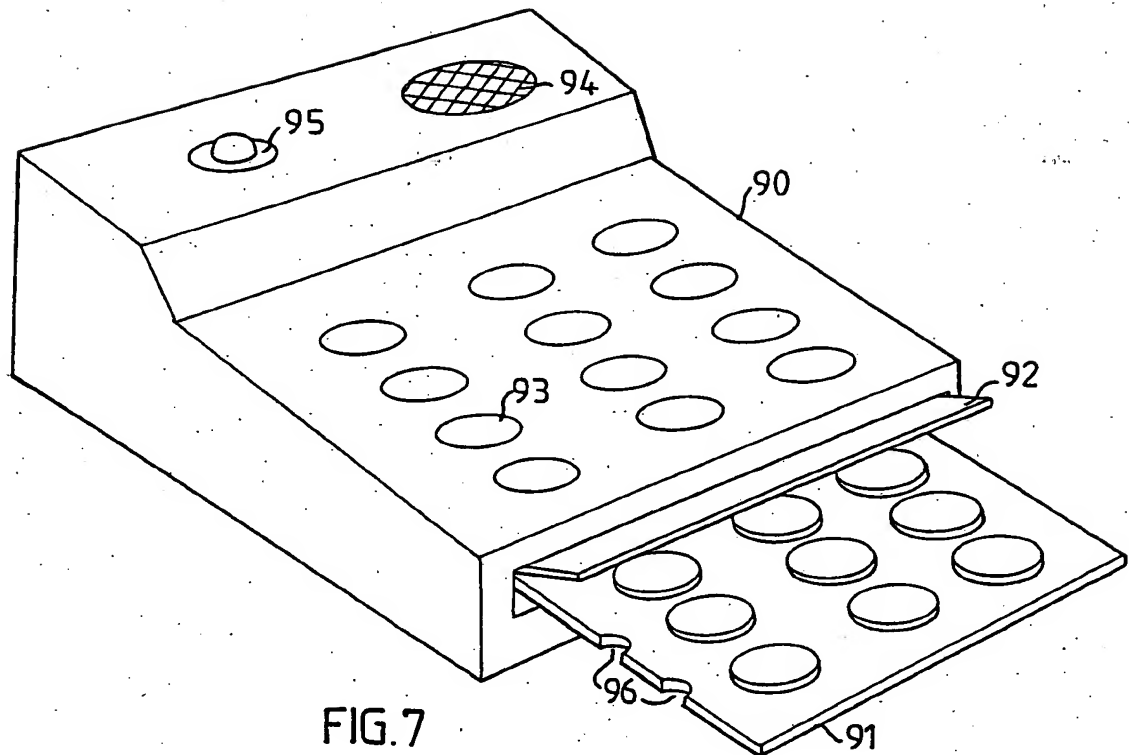
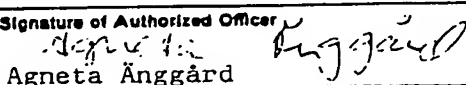


FIG. 7

SUBSTITUTE SHEET

# INTERNATIONAL SEARCH REPORT

International Application No. PCT/SE89/00162

<b>I. CLASSIFICATION OF SUBJECT MATTER</b> (if several classification symbols apply, indicate all) <sup>6</sup> According to International Patent Classification (IPC) or to both National Classification and IPC <sup>4</sup> A 61 J 7/00		
<b>II. FIELDS SEARCHED</b> <div style="text-align: right; margin-right: 100px;">Minimum Documentation Searched <sup>7</sup></div>		
Classification System <sup>1</sup>	Classification Symbols	
IPC 4 US C1	A 61 J 7/00 ; G 04 G 15/00 <u>222-205</u>	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched <sup>8</sup>		
SE, NO, DK, FI classes as above		
<b>III. DOCUMENTS CONSIDERED TO BE RELEVANT <sup>9</sup></b>		
Category <sup>10</sup>	Citation of Document, <sup>11</sup> with indication, where appropriate, of the relevant passages <sup>12</sup>	Relevant to Claim No. <sup>13</sup>
X	EP, A2, 0 191 168 (SIMON UDO) 20 August 1986 & DEU, 8503564 DE, 3530356 JP, 61185267 US, 4660991	1-6
A	GB, A, 2 198 425 (PYXIS CORPORATION) 15 June 1988	1-6
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<b>IV. CERTIFICATION</b>		
Date of the Actual Completion of the International Search  1989-05-09	Date of Mailing of this International Search Report  1989-06-01	
International Searching Authority  Swedish Patent Office	Signature of Authorized Officer  Agneta Änggård	

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